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ONLINE YOGA FOR CHILDREN WITH FUNCTIONAL GASTROINTESTINAL
DISORDERS: A RANDOMIZED CONTROL TRIAL

A Thesis Presented To
The Faculty of the School of Medicine
Yale University

In Candidacy for the degree of
Master of Medical Science

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Abbreviations

FAPDs: Functional Abdominal Pain Disorders

IBS: Irritable Bowel Syndrome

FD: Functional Dyspepsia

AM: Abdominal Migraine

FAD-NOS: Functional Abdominal Pain- Not Otherwise Specified

SMC: Standard Medical Care

FODMAP: Fermentable oligosaccharides, disaccharides, monosaccharides and polyols

CAM: Complementary Alternative Medicine

CBT: Cognitive Behavioral Therapy

FPS-R: Faces Pain Scale-Revised

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ABSTRACT

Functional abdominal pain disorders are characterized by disordered bowel motility and hypersensitivity without organic cause. Children who meet the criteria for functional abdominal pain disorders have difficulty managing abdominal pain due to a lack of effective pharmacotherapeutic options. Several in-person alternative therapies have been beneficial for this population, including yoga. However, access barriers and lack of flexibility in therapy structure result in low adherence. **We propose a randomized controlled trial to study the effectiveness of a 12-week online yoga course compared to a treatment-as-usual group on abdominal pain intensity for children with functional abdominal pain disorders.** We will measure abdominal pain intensity using an average weekly Faces Pain Scale-Revised score at baseline, post-intervention, and 6 and 12-months follow-up. This study will evaluate the efficacy of an accessible alternative therapy that may better address abdominal symptoms in children and lower the risk of future anxiety, depression, and chronic pain.

CHAPTER 1: INTRODUCTION

1.1 Background

1.1.1 Children with Functional Abdominal Pain Disorders

Functional Abdominal Pain Disorders (FAPDs) are a group of conditions affecting the gut-brain axis and are categorized together under the Rome IV diagnostic criteria. Disorders under FAPDs include Irritable Bowel Syndrome (IBS), Functional Dyspepsia, Abdominal Migraine, and Functional Abdominal Pain-Not Otherwise Specified (FAP-NOS).^{1,2} IBS is the most common FAPD.³ FAPDs are a group within the larger Functional Gastrointestinal Disorder family, which are characterized by the lack of organic cause (ie. No clear sign of a pathology on usual testing).^{4,5} FAPDs are differentiated from each other based on the area of the gastrointestinal tract most affected and other associated symptoms.⁶ It is possible for one individual to have more than one FAPD.⁷ FAPDs are typically diagnosed clinically by a patient's primary care provider or a gastroenterologist after ruling out all organic causes⁸ and with symptoms persisting for at least 2 months.¹

The etiology of FAPDs is not completely understood, but it is likely that a combination of genetic, psychosocial and environmental factors predispose certain individuals to be more sensitized to visceral stimuli, leading to a dysregulated relationship between the central nervous system and the gastrointestinal tract.^{4,9,10} After several episodes of pain and disordered bowel motility, the individual enters a cycle where the stress of avoiding a painful episode worsens the underlying functional disorder, leading to more pain episodes.¹ One study found that patients with an FAPDs who had anxiety at baseline were more likely to still have FAPD symptoms at follow-up,

suggesting the central nervous system and gastrointestinal system interact bidirectionally in individuals with FAPDs.¹¹

FAPDs are the most common cause of chronic abdominal pain in children and adolescents, with a meta-analysis concluding that up to 13.5% of children and adolescents suffer from symptoms that meet the diagnostic criteria for a FAPD.³ The same study found that FAPDs affected predominately females, and that the prevalence of FAPDs did not differ between children under 12 years old and children 12 years and older.³ Another study found that over 50% of new patients arriving to a pediatric gastroenterology clinic had one or more Functional GI Disorder, with the majority being FAPDs.¹²

Children with FAPDs often have a reduced quality of life due to their unpredictable and abdominal pain and bowel movements. One study found that children with FAPDs on average scored significantly lower on the health-related Pediatric Quality of Life Inventory than their healthy peers, and scored around the same as children with organic abdominal pain disorders like GERD and Inflammatory Bowel Disease.¹³ In the same study, it was discovered that the parents of children with FAPDs scored their children's quality of life lower than their own children did, suggesting that children with FAPDs may not be entirely aware of how much their quality of life is lowered by their condition.¹³

A unique challenge to the pediatric population with FAPDs is the issue of school absence. Children with FAPDs are more likely to miss multiple days of school in a single school term most often due to abdominal pain,¹⁴ leading to difficulties maintaining peer relationships and participating in school sports and clubs.¹⁴⁻¹⁶ This loss of time in school

further lowers children with FAPDs' quality of life by making them feel isolated from their healthy peers.

The burden of FAPDs often extends beyond the child, with hospital admissions, doctor appointments, and expensive therapies creating a costly and time-consuming burden on the entire family and healthcare systems.¹⁷

The literature on treatment of FAPDs in children is slim, due to the ethical challenges surrounding testing pharmacological treatments on the pediatric population, and limitations to allow children to participate in clinical trials.¹⁵ The studies that do manage to evaluate treatments for this population are low in quality due to small study sizes, being nonrandomized or having conflicting results.¹⁸ Therefore, treatment options for children with FAPDs are limited.

Treatment usually begins with general patient education and reassurance.³ From there, treatment is focused on the patient's specific triggers and symptoms. While the initiation of a low FODMAP diet is common in adults, there is not enough evidence to prove that diet changes are useful in controlling FAPDs in children.¹⁹ Other dietary changes such as adding fiber and probiotics also have low evidence of lowering abdominal pain and associated gastrointestinal symptoms.^{20,21}

Pharmacological treatments for FAPDs are often focused on which part of the gut-brain axis is disordered in an individual, resulting in certain drug treatments working better for some FAPDs than others. The two FAPDs with the most pharmacological research are IBS and Functional Dyspepsia (FD), while Abdominal Migraine (AM) and FAD-NOS have little research data regarding pharmacological treatment.¹⁸ New prokinetic and anti-inflammatory drugs show promise in lowering abdominal pain

severity and frequency, however the placebo groups in these trials also saw improvement, and not all studies found a statistically significant improvement.^{18,22} A systemic review found that antidepressants may have no better improvement in abdominal pain in children with FAPDs than placebo groups, and higher quality evidence is needed to determine their role in FAPD treatment.²³ Non-pharmacological therapies such as gastric electrical stimulation (GES) and percutaneous electrical nerve field stimulation (PENFS) have shown improvement in associated FAPD symptoms like early satiety, bloating and vomiting, however these studies had small sample sizes and small effect sizes, and the long term placement of a stimulator is an invasive procedure.^{24,25}

As children with FAPDs grow up, there is concern that the lack of therapies that provide long-term improvement in symptoms could result in an increased risk of chronic pain, anxiety and depression in adulthood.^{11,26} One 15-year prospective cohort study found that participants with FAPDs as children that persisted into adulthood were at an increased risk of headache and chronic non-abdominal pain.²⁷ Another study found that even if symptoms of FAPDs do not continue into adulthood, children with FAPDs are at an increased risk of psychiatric disorders.²⁸ Therefore, finding other treatment routes for children with FAPDs that can show long-term improvement in symptoms is critical to their future physical and emotional health.

While in the past parents have been cautious to let their children try alternative or psychosocial therapies for FAPDs due to either believing negative myths surrounding them or thinking they won't work²⁹, the popularity of Complementary and Alternative Medicine (CAM) therapies has been rising in pediatric patients with chronic pain conditions that are overall challenging to treat with diet and medication.³⁰ In one study

from children visiting pediatric gastroenterology clinics in the Netherlands, CAM was shown to be more popular among pediatric patients with functional disorders than organic disorders, and the parents of these patients felt that CAM being initiated by their child's pediatrician was an essential part of their child's treatment.³¹

1.1.2 Yoga as a Therapy for Children with FAPDs

One type of CAM that is becoming popular among all age groups, healthy and not, is yoga. Yoga originated in India over 4000 years ago, and has remained in society due to its ability to reduce stress and anxiety, and relax multiple muscle groups without requiring expensive tools or high skill level.³² More specifically, yoga has been shown to improve muscle flexibility and strength, blood circulation, and could even alter hormone release and function.³³ As a result, the bodies of those who consistently practice yoga are better prepared for stressful situations, including illness, chronic pain, and cardiovascular disease.³⁴ Another benefit of yoga is that it is a fairly safe therapy, with the recorded side effects being only related to musculoskeletal injury from overstretching or falling from a balancing position. These results can be minimized easily with the use of proper technique and supervision.³⁵

Yoga has many different branches of technique, with some being more beneficial for certain groups. Hatha yoga is a common yoga type in North America, and one of its most popular branches is called Iyengar. Iyengar yoga is comprised of a series of stationary poses, with breathing and meditation done in each pose. This type of yoga has become a common form to use among those with chronic medical conditions, as it combines mental and physical relaxation techniques.¹⁶

Stress impacts the body and mind in multiple ways, not only causing physical tension, but creating a mental obstacle in the way of relaxation and comfort. Yoga can provide relief for children currently living in a very stressful and sedentary world.³³ In fact, it is the fifth most common type of CAM therapy in use among children aged 2-17. It is already a common adjuvant to children with chronic pain, with 32% of children considering their top choice for CAM therapy.³⁶

With Iyenger yoga's focus on both mind and body relaxation, and the relative ease of implementing yoga therapy into a daily routine, researchers have begun to examine the efficacy of yoga therapy for symptom improvement for children with FAPDs. Several studies have found that yoga sessions for as little as 1 month could significantly improve abdominal pain and anxiety, with improvements still being seen 3 months post-intervention period.^{16,37}

Another common trend seen in past studies of pediatric patients with FAPDs utilizing yoga therapy is the importance of home practice on the initial and sustained response to treatment. Teen participants with IBS who responded well to yoga therapy noted in follow-up surveys that they practiced yoga at home, and that home-practice would be necessary to reap the maximum benefits of yoga therapy.³⁶ In studies where home-practice was not mandatory but suggested as a way to achieve long-term symptom relief, participants were more likely to practice yoga when they felt abdominal pain.³ In 2012, a survey of yoga practitioners noted that home-practice was a better indicator of improved health outcomes and quality of life than attending actual yoga classes.³⁸

While yoga is a relatively safe and easy therapy to learn, there is still the added cost and time burden of attending in-person yoga classes that is similar to other FAPD

treatments. When asked about the possibility of continuing the yoga therapy for a longer time period, both parents and participants of one study expressed frustration with the amount of time being spent traveling, and how that time could be better spent in extracurricular activities or caring for other members of the family. This sentiment was expressed among those traveling short and long distances.³⁶ This burden was often reflected in the adherence to therapy in all studies looking at yoga therapy for children and adolescents with FAPDs, with no studies having 100% participation in all yoga sessions and the loss to follow-up being as high as 32.9% in one study.³⁹ Another possibility for low adherence is the lack of flexibility in class structure, which may be difficult to children to stay engaged in for more than a few sessions.

1.1.3 Utilizing Online Therapies for Chronic Illness

Today's children and adolescents are incredibly adept at accessing and using technology in a number of different ways in daily life. This is likely due to the increasing number of households in the United States with internet access. According to the U.S Census Bureau in 2016, 76% of American households had at least 1 smart phone, with the majority also having a tablet, laptop or desktop. The majority of low-income households have access to at least one internet-capable device.⁴⁰ The "digital divide" in internet use between non-Hispanic Whites and minority groups also continues to close, with the proportion of Hispanic Americans using the internet increasing from 49% in 2010 to 72% in 2017 and proportion of African Americans using the internet increasing from 59% in 2010 to 73% in 2017.⁴¹ The statistics show that moving traditionally in-person therapies to the internet could be a way to make treatment options more accessible to

those who typically cannot participate due to the expense of the therapy or the need for transportation to classes and appointments.

With the Covid-19 pandemic resulting in the inability to meet in-person, telemedicine and teletherapy became the new normal for many patients around the world. Nearly 2 years since the first lockdowns, the impact of at-home yoga therapy for the pediatric and adult population are being studied as a possible permanent fixture in medicine. Studies have shown that benefits from teletherapy include treating patients in remote areas, increasing free time for school, work and activities, and reducing overall treatment costs.⁴²

Yoga therapies for cancer patients that were initially started in-person and then transitioned to online only due to the pandemic were still deemed effective by participants, and many participants also wished to continue tele-yoga even after in-person therapies were safe again.^{43,44} A school in India that previously taught in-person yoga during the school day found that children were still able to receive the same mental and physical benefits from video-call yoga during the pandemic.⁴⁵

There is a lack of research into online therapies for children with chronic pain conditions,⁴⁶ and available studies are low in quality.⁴⁷ For children with FAPDs, the only online alternative therapy to be investigated so far is cognitive behavioral therapy (CBT), with several studies finding participants randomized to receive CBT had improved gastrointestinal symptoms and anxiety, resulting in lower treatment costs overall.^{42,48,49}

1.2 Statement of the Problem

Children with FAPDs currently have limited forms of treatment that are safe and effective, resulting in the increased intensity of abdominal pain and a high rate of school

absenteeism. Poorly controlled symptoms may lead to future chronic pain and psychiatric disorders in adulthood, therefore finding effective long-term treatments for this age group is critical.^{11,26} Alternative therapies like yoga offer a possible way to alleviate abdominal pain and increase school participation and quality of life, however driving children to yoga sessions can create extra burden for parents and reduce time for children to participate in other activities.³⁶

Several systematic reviews of the literature mention that the evidence for yoga being a beneficial therapy for children with FAPDs is moderate to low in quality, due to sample population sizes being small, and with participant drop out from studies being relatively high, especially among those placed in control groups.^{50,51} These studies also had rigid and long yoga regimens that may not be well suited for children, possibly contributing to the low adherence rates. One study suggested that better tailoring of the yoga instruction may improve adherence, especially for children and adolescents.³⁹

There is also discrepancies between studies concerning how often yoga should be practiced, and how long the study period should be. The practice per week ranged from daily to once a week, and the study periods ranged from four weeks to a current study underway that has its study period lasting eight months.⁵² The follow-up periods were also often only a few months from the end of the study period. Having a significant amount of time between yoga sessions may be associated with less than ideal levels of adherence, and having a short study period may not be long enough to see the full impact of the therapy, and may hinder the goal of long-term symptom relief.

The rise in effective tele-therapies for children with chronic conditions including FAPDs is a promising accessible alternative to in-person therapies, however online yoga

for children with FAPDs has not been investigated. Therefore, we propose a randomized controlled trial (RCT) to evaluate the efficacy of an online, interactive and child-friendly 12-week yoga course as an adjunctive therapy to standard medical care (SMC) in children with FAPDs.

1.3 Goals and Objectives

The overall goal of our study is to provide an alternative therapy for children with FAPDs whose symptoms are not well controlled with only medications and reassurance. Our first objective is to determine the efficacy of an online, interactive yoga course in addition to standard medical care on the pain intensity scores of school-aged children with functional abdominal pain disorders compared to those only receiving standard medical care. Our second objective is to determine if a more child-friendly yoga program (use of imagery, participant choice of moves and their order) with less familial burden will affect adherence and/or loss to follow-up.

1.4 Hypothesis

Among school age (8-12) children with Functional Abdominal Pain Disorders (FAPDs) participating in a 12-week online yoga intervention, there will be a statistically significant change in abdominal pain intensity, as determined by mean change in abdominal pain intensity score from baseline to 12-month follow-up, compared to those only receiving standard medical care.

1.5 Definitions

Online Yoga Intervention: A 12-week yoga program delivered via a website that only participants randomized to the intervention group will have access to. Online yoga will be

performed at least three times a week for 30 minutes per session. Participants will have the option of choosing 10 movements from a list of 20 in the order they prefer.

Abdominal Pain Intensity Score: Derived from the Faces Pain Scale-Revised (FPS-R), participants will score their pain intensity on a scale of 0-10 three times daily for one week at baseline, week 12 of intervention and at 6 and 12-month follow-up, with scores from one week being averaged into a mean Abdominal Pain Intensity Score.

Standard Medical Care: A child's typical treatment plan established prior to recruitment for this study, including current prescribed medications, diet regimens, and annual visits to a gastroenterologist who provide reassurance and education.

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CHAPTER 2: REVIEW OF THE LITERATURE

2.1 Introduction

An extensive review of the literature was conducted between August 2021 and May 2022 using PubMed, Ovid Medline, Scopus, and Cochrane Review. All articles were published after 1998, with the majority of articles published after 2014. Articles were only read if they were published in English and the abstracts provided evidence for relevance to our proposed study. Key terms used on each database for the primary search were: *Children, School-Age Children, Pediatrics* combined with *Functional Abdominal Pain Disorders, Irritable Bowel Syndrome, Functional GI Disorders, Functional Dyspepsia, Functional Abdominal Pain*, combined with *yoga, mindfulness yoga, remote therapy, internet-based intervention, online therapy, computer-based therapy* combined with *Faces Pain Scale, School Absence, Quality of Life, Pain Measurement, Severity of Illness Index*.

Studies read and analyzed included clinical trials, systematic reviews, meta-analyses and randomized controlled trials. Secondary searches widened the population to adults with FAPDs and to children with FAPDs who received other types of alternative therapies, both online and in-person. No randomized controlled trials examined children with FAPDs using online yoga as an intervention.

2.2 Review of Empirical Studies

2.2.1 Yoga as an Intervention for Adults with FAPDs

Yoga as an intervention for patients with functional abdominal pain disorders was first investigated in the adult population, with the majority of studies focusing only on patients with irritable bowel syndrome, likely due to being the most prevalent FAPD.¹

Four randomized controlled trials were identified. While they vary in population age, adherence and outcome measure, they all found that a form of yoga intervention was significantly helpful in improving one or more aspects of a patient's life.

The first study was published in 2000 by Ragahavan et al., whose pilot study examined 7 young adults randomized between a 4-month yoga intervention and waitlist control. The study found those in the yoga intervention experience lowered illness perception and improved well-being, however there is no mention of what outcome measures were used. Despite an incredibly small sample size and no analyses due to lack of funding, this study opened the door to further exploration of this alternative therapy.²

The next study was published in 2004 by Taneja et al. and investigated a yoga and right nostril breathing intervention compared to a symptomatic treatment control of loperamide in 22 male adults with IBS-diarrhea predominant.³ This study's primary outcome measure was autonomic symptom score, which included abdominal pain. Symptom absence was a score of 0, while a patient who exhibited all 10 symptoms included in the survey scored a 10. The intervention period lasted 2 months with no follow-up. While both groups demonstrated improvement, statistical analysis showed that autonomic symptom scores significantly improved more in the yoga and nose breathing intervention compared to those randomized to the symptomatic treatment group ($p < .05$). This study has many limitations, including the recruitment of males only, when it is known that irritable bowel syndrome is more prevalent in women.⁴ The sample size is small, and there is no mention of how the two groups were randomly allocated. Finally, the patients were instructed to practice yoga twice a day for the entire intervention period,

which is a very intensive dose and frequency of intervention, and it is unknown how many of the participants adhered completely to this regimen.³

Later studies with yoga intervention in this population were much more detailed about the different aspects of the yoga intervention and control groups, measure of outcomes, and level of adherence to therapy. In 2016, Shahabi et al. conducted a pilot RCT with 35 adults aged 18-65 with IBS who were randomized to either a 16-week yoga intervention that consisted of 8 in-person yoga sessions, or a 16-week walking program.⁵ The primary outcome was a gastrointestinal symptom and abdominal severity survey, with a score of 0 indicating no symptoms or pain in the past week and 21 indicating maximum symptoms and pain in the past week. Scoring was completed pre-intervention, post-intervention, and at 6-month follow-up.⁵ Analysis revealed that both the yoga intervention and walking intervention significantly improved different aspects of the primary outcome post-treatment ($p < .05$). However, only the walking group continued to experience the benefits of their therapy at the 6-month mark. This could be related to the differing percentage of participants continuing their assigned therapy at 6-month follow-up, with 50% of the yoga intervention saying they practiced yoga at home in the last month versus the 100% of the walking group saying they had walked at least once in the last month. These results may also be altered by the loss to follow-up during and after the treatment period. Five participants from the yoga group and three participants from the walking group withdrew from the study, citing difficulty in finding reliable transportation, length of transportation time, and changing schedules. Additionally, only 74% of the participants who completed the treatment period filled out surveys at the 6-

month follow-up. Therefore, this study lacks a strong argument for the efficacy of yoga versus walking therapies.⁵

Schumann et al. in 2017 compared adults ages 18-75 with IBS in a twice-weekly yoga class with progression in difficulty and intensity, to a low FODMAP diet plan that had both an elimination and reintroduction phase.⁶ The intervention period was 12 weeks with a 12-week “follow-up” period, with the FODMAP group using the intervention period as their food elimination phase, and the follow-up period as the food reintroduction phase, giving 2-3 days to challenge a FODMAP food. The primary outcome was Irritable Bowel Syndrome-Symptom Severity Score (IBS-SSS) by assessors blinded to participant group assignment.⁶ While this score significantly decreased after the intervention and follow-up periods in the yoga intervention groups ($p < .001$), this decrease was also seen in the FODMAP elimination group, with no significant difference seen between the groups at post-intervention or post-follow-up periods ($p = .180$). However, there was greater average session participation in the FODMAP elimination group (87.36%) compared to the yoga intervention group (61.94% of the 24 in-person sessions). The FODMAP group only had to attend 3 in-person education sessions compared to the yoga group, which had to attend 24 in-person sessions. This burden on the yoga group may have also contributed to yoga’s lack of improvement over the FODMAP elimination group.⁶

In each of these studies, the limitations of small sample size, unknown or low adherence, and only studying IBS patients reduces their internal validity and their generalizability to the greater adult population with FAPDs. Additionally, half of the studies had active controls, which lessens the ability to adequately compare these studies.

These active controls would also be unlikely to transition well to a child population, resulting in low adherence in the control group.

2.2.2 Yoga as an Intervention for Children and Adolescents with FAPDs

In our systematic literature review, we identified four randomized controlled trials and one single-arm study investigating a yoga intervention in children and adolescents with a range of FAPDs. In 2006, Kuttner et al. recruited 28 subjects aged 11-18 with IBS and randomized them to either receive a yoga intervention involving 1 hour of in-person instruction and four weeks of daily at-home practice or a waitlist control, having participants continue their standard medical care for 4 weeks and then partaking in the intervention the following 4 weeks.⁷ Yoga poses were required to be performed in the same order for each daily session, for a total of 10 minutes a day. Primary outcomes included a 3-question gastrointestinal symptom questionnaire, pain intensity score and functional disability inventory, which is the participant's subjective rating of how their FAPD interferes with daily life. Data was collected at baseline, post-intervention, and after the waitlist control completed their yoga intervention. There was no long-term follow-up for this study.⁷ A p-value of 0.10 was used for the statistical analyses of these results due to the lack of prior evidence in this population. Results showed a statistically significant reduction in functional disability inventory in the yoga intervention group prior to the control group's intervention data being combined. When both groups' yoga intervention data was analyzed, a statistically significant decrease in gastrointestinal symptoms was found. The pain intensity score was removed from the analysis due to baseline differences in scores between the intervention and control groups (4.93 ± 1.74 in the yoga groups versus 6.82 ± 2.40 in the control group). The limitations of this study

include small sample size, lack of follow-up and low adherence to the intervention (yoga frequency score 0-10 with 0="never" and 10="every day," average of 6.81 ± 2.52 out of 10). Even with participants performing the yoga intervention at home, there was still difficulty completing the yoga sessions due to the rigid nature of the program, which didn't allow participants to focus on certain moves they felt helped their specific areas of pain and gastrointestinal symptoms more than others.⁷

Brands et al.'s study in 2011 was the first study to include children age 8 and older alongside adolescents with IBS or Functional Abdominal Pain, a Rome III criteria diagnosis.⁸ The 20 participants were their own control group, continuing their standard medical care for 1 month before the intervention. Their intervention was a 10-session hatha yoga class over 12 weeks that included imagining a good experience, focusing on a single idea, and using animation. The primary outcome was pain intensity and pain frequency, with pain intensity measured using Pain Faces Scale-Revised and the pain frequency score measured as 0 = no daily pain, 1 = 0—20 minutes of daily pain, 2 = 20-40 minutes of daily pain, 3 = 40–90 minutes of daily pain, and 4 = >90 minutes of daily pain. Outcome measures were recorded daily during the SMC control month, one month during the yoga intervention, and the third month post end of the intervention period.⁸ From from baseline SMC month to post-yoga intervention, the pain intensity and pain frequency scores were found to decrease significantly in the 8-11 age range ($p = .031$ and $p = .0015$ respectively), and the pain frequency scores were found to decrease significantly in the 11-18 age range ($p = .004$). Pain frequency scores continued to be decreased in the 8-11 age group at 3-month follow-up ($p = .04$). Despite these promising results, the sample size was small and there was no adherence data. The participants acted

as their own controls, which has benefits to reducing loss to follow-up and controls and intervention having the same baseline characteristics, but there is an increased risk for selection bias without the use of randomization.⁸

Evans et al. conducted a RCT in 2014 examining the effects of a yoga intervention with the use of props and imagery compared to a waitlist control on IBS symptoms via a Child Somatization Score in 51 patients aged 14-26.⁹ The yoga sessions were twice weekly for 6 weeks. Home practice was encouraged but not required. The primary outcome was a reduction in IBS symptoms using a portion of the Child Somatization Inventory, which was found to be significantly decreased after the intervention period and at 2 months follow-up. This study had an average of 9 out of 12 yoga session attendance, and more than 4 times the amount of participants dropped out of the study from the waitlist control group than the yoga intervention group at baseline. Of all the studies in this literature review, this study had the greatest attrition rate at 32.9%. The low adherence may be related to the large burden of traveling to and from the yoga session twice a week. This study brought up the point that when studying a younger population, both the parent and child or adolescent have to be motivated to participate in the study, not just one or the other.⁹

A follow-up study by Evans et al. in 2018 focused on the 14-18 age range of the previous study and investigated the reasons behind why certain participants had multiple benefits from the yoga intervention while others had very few.¹⁰ The greatest difference between these groups was the level of parent commitment to the study. Parents of nonresponders often had to drive the participant an hour or more to reach the yoga session location, taking up valuable time on a weeknight or weekend afternoon that could

be spent at work or caring for another family member. Another finding that was unanimous among all teens randomized to the yoga intervention was that yoga was useful to them in managing their daily IBS symptoms and painful episodes.¹⁰

In 2016, Korterink et al. took aspects of Brands et al.'s study and expanded upon them, including extending the yoga intervention to biweekly for 16 weeks, increasing the sample size to 69, and having a separate randomized control group that received SMC during the 16 week intervention period.¹¹ Follow-up was also extended to 6 and 12-months from baseline. The primary outcome was the same as Brands et al., pain intensity score using the Faces Pain Scale-Revised and a pain frequency score recorded daily for 4 weeks at baseline, post-intervention and follow-ups. There was a significant decrease in pain intensity score and pain frequency score in the yoga intervention when comparing baseline to 12-month follow-up ($p < .01$ and $p < .01$ respectively). The SMC also saw a decrease in pain intensity and frequency but not at a significant level ($p < .83$ and $p < .40$ respectively). At 12-month follow-up, the pain intensity was significantly lower in the yoga therapy than SMC ($p < .04$). While this study attempted to address some of the limitations of Brands et al., they did not measure how many participants continued yoga after the intervention period, and there was no data on adherence to the yoga intervention.¹¹

The most recent study we reviewed was published last year and was by Högström et al., who investigated a yoga and dance combination therapy for girls between the ages of 9 and 13 with IBS or functional abdominal pain according to Rome III criteria.¹² This study had the largest sample size of 121 participants, and the largest intervention period of 8 months. The yoga and dance session is performed twice weekly for an hour, while

the control group continued SMC. Data was collected at the mid and endpoints of the intervention period, and the follow-up period is 2 years long, which is still ongoing. The primary outcome is maximum abdominal pain, calculated by measuring pain scores three times daily for a week using the Faces Pain Scale-Revised, and then taking the highest score from that week. Intention to treat and per-protocol analysis were completed, which both showed the yoga and dance intervention significantly lowering maximum abdominal pain scores more than the SMC group at 4 and 8 month follow-up ($p < .003$ and $p < .002$ respectively). This significant improvement was seen even with class attendance for the yoga and dance group averaging 63% for the first half and 55% for the entire intervention period. With low adherence and the inability to reach the calculated 150 participant sample size needed for this study, this intervention period may be too long and burdensome for both participants and their families.¹²

While many of the studies we reviewed showed evidence that a yoga intervention for children with FAPDs may be effective in improving some aspect of their condition and/or quality of life, all studies had low adherence or no data on adherence at all. Most of these studies also had participants perform yoga in a group session, which could improve scores due to the effects of support from children facing similar issues. Improving adherence to the intervention and eliminating possible group effects may be a way to see more positive effects from yoga in a range of improved outcomes, but changes to the study design will have to be made to address the reasons why participants and their families don't show up to the intervention or withdraw from the study altogether.

2.2.3 Feasibility and Efficacy of Internet-Based Therapies for Children with FAPDs

While studies investigating internet-based interventions for adults have ranged from cognitive behavioral therapy^{13,14} to exposure-based treatments¹⁵ and even hypnotherapy¹⁶ with moderate success, internet-delivered therapies for children with FAPDs have been limited to various forms of cognitive behavioral therapy only. Two RCTs have currently been published for this intervention and population, along with several clinical trials completed as well, but with no results published.

Lalouni et al. in 2019 studied 90 children ages 8-12 randomized to an intervention of 10 weeks of therapist-guided online cognitive behavioral therapy (CBT) or a waitlist treatment-as-usual control.¹⁷ The children in the intervention group completed exposure-based situations in places where they often felt their symptoms and also were taught mindfulness techniques and symptom-controlling strategies. Parents were encouraged to praise their children for good coping behaviors and lower attention to bad coping behaviors, such as complaining about symptoms. A therapist was available via text message to help guide the child and parent through the intervention and to provide support. The primary outcome was scoring on the PedsQL Gastrointestinal Symptoms Scale, which was administered at baseline, post-intervention and 36-week follow-up. The online CBT participants were more likely to have a clinically significant improvement of 30% or more on the PedsQL Gastrointestinal Scale than the waitlist treatment-as-usual control (58% of internet CBT group versus 32% of the waitlist control group). While this study was strong due to low attrition rates and high adherence to the intervention, limitations included the crossover control group to intervention, which may have created some expectation bias that the internet-CBT intervention would be superior to treatment-

as-usual. This study also showed that internet-delivered therapies could be a feasible low-cost option for those who cannot afford expensive in-person alternative therapies.¹⁷

Walker et al. in 2021 further built upon Lalouni et al. by having a control group receive online patient education while the intervention group received online lessons about pain coping skills with interactive activities that a health coach would provide feedback on.¹⁸ The study recruited 278 participants between the ages of 11-17. This study was able to be double-blinded due to only telling participants that they would be randomized to 1 of 2 websites, without informing them of the differences between websites. It was also unique in dividing participants into three groups based on symptom severity and stratifying by these groups when randomizing the intervention and control. The primary outcome was GI symptom severity using the Children's Somatic Symptom Inventory (CSSI). Data collection was at baseline, after the intervention period of 8 weeks, 6-month follow-up and 12-month follow-up. Participants in the highest symptom severity group had a significant improvement in CSSI score from baseline to post-intervention compared to the control group, however improvements were seen in both groups in the other two symptom severity groups, and in all groups at 6 and 12-month follow-up. Strengths of this study include the large sample size and the double-blind design. While having an active control group limited the loss to follow-up in the control group, not having a true control group limits these results from being generalized to a population with standard medical care.¹⁸

While both of these studies addressed the need for more accessible formats of alternative therapies, one study may have had high adherence due to expectation bias,¹⁷ and the other had significantly more active controls complete their education modules

than the internet-CBT intervention group ($p < .001$).¹⁸ This emphasizes the need for an intervention that is engaging and flexible for children to enjoy while participating.

2.3 Identifying Confounding Variables

During our review of the literature, we identified multiple confounding variables that were both controlled for and not controlled for.

Many studies had a wide range of ages recruited for the study, with age groups then split when analyzing the results. These age groups often had different results from each other, such as Brands et al., which saw the 8-11 age group have more significant improvements on several outcome measures compared to the 11-18 age group.⁸ Evans et al. saw a similar difference between their 14-17 age group and their 18-26 group, with the older age group having more significant improvements.⁹ Korterink et al. mentioned an age group difference for one of the primary outcomes but never mentioned the age groups again.¹¹ These studies did not agree on which age group had a more effective response to yoga therapy, which only leads to confusion about how to interpret these results. Our proposed study will have a smaller age range of ages 8-12 to better focus on the results from a specific age group.

A majority of the yoga intervention studies had participants perform yoga in small groups, while the control participants continued standard medical care alone. For a population who often feels isolated from social environments¹⁹, this introduction to a social circle could have more impact than a healthy child. These group yoga sessions could have confounded results, as the encouragement and social support may have led to more significant improvements in abdominal pain, gastrointestinal symptoms and quality

of life.^{5,12} Our study, similarly to the studies investigating internet-CBT^{17,18}, will be mostly an individual therapy except for the initial yoga learning session.

Other possible confounding variables have been controlled for in previous studies and will be included in our study, such as gender, Rome IV diagnosis, duration of symptoms, other functional symptoms and household income.¹¹ Evans et al.'s studies were the only studies reviewed to note participant race.^{9,10} We include participant race in an effort to monitor the diversity of our study. Baseline measures of the primary and secondary outcomes will also be analyzed to make sure there are no significant between-group differences, as was seen with pain intensity in Kuttner et al.^{7,9,12}

Another possible confounder to results in the studies reviewed is adherence level. Many of the studies investigating a yoga intervention for children with FAPDs were limited by low adherence to the intervention, with the lowest participation seen in Evans et al.⁹ There was no investigation into if rates of efficacy in the intervention group were higher in those with greater adherence. Our study aims to raise adherence by providing a more interactive at-home yoga therapy, increasing the participation of participants.

2.4 Review of Relevant Methodology

2.4.1 Study Setting and Design

The proposed study will be a two-arm randomized controlled trial, which a majority of the studies we reviewed also utilized. One study used a single-arm non-randomized study design approach to try and reduce loss to follow-up. Brands et al. had their participant group act as their own control group for a month prior to the yoga intervention.⁸ This design has many limits, including lack of randomization, expectation bias, and the inability to monitor for a possible placebo effect.²⁰ Several studies used a

waitlist control group to try and reduce loss to follow-up, but this created expectation bias among the control group, as they expected the intervention they were waiting for to be more effective at improving their symptoms than the current regimen they were already on.^{7,9,17} Our proposed study will not have a waitlist control group, but rather the control group will have access to the intervention materials after all follow-up data is collected, similar to Högström et al.¹²

In order to recruit enough participants, our proposed study will be a multi-center trial, recruiting participants from two large gastrointestinal specialty clinics. Most of the studies reviewed had participants recruited from gastrointestinal centers, with a majority of the earlier studies only recruiting from one center. As many of these studies were pilot studies, having a small sample population to recruit from was less of a concern than later studies, with Högström et al. having to extend their recruitment time and still not managing to reach their goal sample size of 150.¹²

A variety of randomization strategies were used by the RCTs we reviewed. All studies used a 1:1 allocation. A majority of studies used block randomization, with some additionally stratifying blocks by age,¹¹ history or non-history of depression,⁶ or symptom severity.¹⁸ Most studies had randomization completed by an outside statistician or research assistant not involved in the rest of the study. This allows for blinding of participant allocation to the other research staff. Our study will use block randomization stratified by duration of symptoms in months. We will have a separate research assistant in charge of block assignment and accessing the computer database that will randomly place participants into either an online yoga with SMC group or just SMC group.

2.4.2 Selection Criteria

Inclusion and exclusion criteria will be similar to the studies we reviewed involving children with FAPDs. Brands et al. excluded children who have participated in other alternative therapies, including hypnotherapy, relaxation therapy, psychotherapy or yoga therapy.⁸ Evans et al. further excluded children who had an organic gastrointestinal disorder in addition to a FAPD.⁹ Korterink et al. then excluded children with FAPDs who could not follow instructions well, as yoga instruction would be given verbally with children intended to follow commands.¹¹ Lalouni included criteria that all participants needed to be stable on any prescribed medication for at least 1 month, and that stable internet access would be needed.¹⁷ All studies required the participants to be fluent in the language in which the research was being conducted.

2.4.3 Intervention

The in-person yoga instruction varied greatly in length of session, with 1.5 hours being the longest⁸ and 10 minutes being the shortest.⁷ The number of yoga sessions per week also varied, with the least frequent being a biweekly program^{5,11}, and the most frequent being Taneja et al.'s study requiring yoga at home twice daily.³ The length of the intervention period could be as short as 4 weeks⁷ and as long as 8 months.¹² Finding the right frequency and length of online yoga intervention is important to maintaining adherence and seeing results. Our proposed study will use a 12-week online yoga program that lasts 30 minutes and is required 3 times a week.

The content of the yoga intervention is also very important in retaining participants. Lack of adherence in the yoga intervention groups of previous studies could be related to a yoga style and delivery that did not have a child's attention span in mind.

To create a child-friendly online yoga program, we will incorporate aspects of Brands et al.'s program of Hatha yoga with animation and the use of imagery to help participants stay engaged in the session and to want to return for another session.⁸

2.4.4 Content of Control Condition

Our control condition will be standard medical care, which will include the regimen of pharmacotherapy, diet and clinician support that the participant was already using before being recruited for our study. While several studies used an active control^{3,5,6}, this limits the ability to measure for placebo effect and to see the true effects that an intervention can have on this population. Our intervention is a novel combination of both yoga and online-directed care, and so the use of a treatment-as-usual group is appropriate when testing a new intervention.⁹

2.4.5 Outcome Measures

The primary outcome measure for our study will be a pain intensity score, calculated using the Faces Pain Scale-Revised,²¹ which will be measured three times a day for one week at certain time points. Our measurement timing is based on Högström et al., who also used Faces Pain Scale-Revised, but instead of averaging the weekly score, they averaged the maximum pain score each day into an average maximum pain score for the week.¹² This pain scale has been validated in children and is comparable to other validated pain scale measures.^{22,23} Our proposed study is investigating the mean pain intensity score change from baseline to 12-month follow-up.

Our secondary outcomes include quality of life, school absenteeism and pain frequency score. Quality of life will be measured using the PedsQL Gastrointestinal Symptom Module, which is a valid survey for measuring the quality of life in children

ages 8 and up.²⁴ Lalouni et al. used the PedsQL Gastrointestinal Symptom Scale, which is similar to the module version but with fewer items. There was a significant improvement in PedsQL Gastrointestinal Symptoms Scale score in the internet-CBT group compared to the treatment-as-usual group.¹⁷

School absenteeism will be measured as the proportion of children who missed more than 1 day of school for FAPD-related reasons in 1 month. This measure was used in Korterink et al., where the yoga intervention saw significant improvement in this outcome.¹¹

Pain frequency will be measured on a previously used pain frequency scale. In the previous times this pain frequency scale has been used, it was combined with a pain intensity score to create an abdominal pain score.^{8,11} For our study, we decided to use only the pain intensity score as the primary outcome, as it had a validated scale in place.

2.4.5 Review of Sample Size and Calculation Power

The common thread among all of the studies we reviewed was that study sample sizes were often too small to make any large statements about the study's results. Our proposed study aims to recruit 142 participants, which will be a large enough sample size to accurately see the effect of our online yoga intervention on pain intensity scores.

The expected effect size for mean change in pain intensity score from baseline to 12-month follow-up between intervention and control groups is 1.62 ± 2.97 . This effect size reflects an expected 52.9% decrease from baseline pain intensity score in the intervention group and an expected 25% decrease from baseline pain intensity score in the control group found by Korterink et al.¹¹ The assumed baseline pain intensity score derived from the Faces Pain Scale-Revised of 5.80 was found by Lalouni et al.²⁵ This

results in an expected mean change in Pain Intensity Score of 3.07 in the intervention group and 1.45 in the control group. The mean change in the intervention group is greater than the minimally clinically significant difference of 2 on the Faces Pain Scale-Revised calculated by Tsze et al.²⁶ To detect an effect size of 1.62 ± 2.97 in mean change in baseline Pain Intensity Score, 106 participants would be needed with 53 in each arm, according to the Statulator Statistical Calculator.²⁷ This is greater than the recommended minimum of 50 participants per arm for clinical trials studying interventions related to pain relief determined by Moore et al.²⁸

To correct for loss to follow-up, the most conservative attrition rate of the reviewed studies, 32.9%, was assumed.⁹ Therefore, an additional 36 participants were added for a total of 142 participants total with 71 in each arm.

2.5 Conclusion

While there is evidence to suggest that an adjunct yoga intervention to standard care in both the adult and pediatric FAPD population may be efficacious, the evidence is often lowered in quality due to lack of adherence and loss to follow-up in both the intervention and control groups. This lowered participation in previous studies is often attributed to difficulties finding transportation, long travel times, increased burden on families, changing schedules, boredom with the intervention, or unwillingness to be the control. Online cognitive behavioral therapy has been studied in this population with positive effect, but these studies are limited by biases and/or lack of standard medical care control group. Our study looks to a novel therapy, the use of an online and interactive yoga therapy, to be more efficacious in reducing abdominal pain and

improving the quality of life for children with FAPDs. The effective study designs and methods presented in this literature review will be incorporated into our study.

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CHAPTER 3: STUDY METHODS

3.1 Study Design

Our proposed study will be a multi-site, two-arm and single-blinded randomized controlled trial. We will be evaluating the effects of an online interactive yoga course as an addition to standard medical care on mean pain intensity scores among children with functional abdominal pain disorders. Our multi-site study will recruit participants from two gastroenterology clinics in New Haven and Hartford County. Eligible children will be randomly assigned (1:1 allocation) to the online yoga therapy intervention or a standard medical care control group by block-randomization prior to the baseline assessments. Children in the online yoga therapy group will continue with their current treatment plan alongside yoga. The intervention period will last for 12 weeks, with data collected at the start and end of this period and at 6 and 12-months following the end of the intervention period.

3.2 Study Population and Sampling

The source population will be children aged 8-12 years old at the time of recruitment receiving care from two outpatient gastroenterology centers in New Haven and Hartford County with symptoms meeting the Rome IV diagnostic criteria for a functional abdominal pain disorder. From those who respond to recruitment materials and referrals, participants will be chosen based on set inclusion and exclusion criteria. Participants will be added to the study via convenience sampling until an adequate number of participants is reached, or the end of the recruitment period is reached.

3.2.1 Inclusion Criteria

Inclusion criteria will include age of 8-12 at time of recruitment, diagnosed FAPD according to Rome IV criteria, stable dosage of any medication for at least 1 month, and home internet access via an electronic device owned by the participant or member of the participant's family. Participant fluency in English will be required as yoga instruction will be provided in English only. Participants also may only be included in the study if they have parent or guardian consent. All inclusion criteria must be met to participate in the study.

3.2.2 Exclusion Criteria

Exclusion criteria include children who have previously used any type of relaxation therapy (Yoga, Hypnotherapy, Cognitive Behavioral Therapy or mindfulness/meditation), have been diagnosed with an organic gastrointestinal pain disorder or have difficulty following instructions. Any participants already enrolled in a different clinical trial will also be excluded.

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Age 8-12 at time of recruitment	Diagnosis of organic gastrointestinal disorder
Diagnosed with a FAPD per Rome IV criteria	Previous use of relaxation therapy including: -Yoga -Hypnotherapy -Cognitive Behavioral Therapy (CBT) -Mindfulness/Meditation
Home internet access via electronic device	Difficulty following instructions due to developmental or learning disability
Fluency in English	Current enrollment in another clinical trial
Consent from Guardian	Current or Future Hospitalization

3.3 Recruitment

The study population will be recruited from the Yale Pediatric Gastroenterology Outpatient Center and the Connecticut Children’s Center for Neurogastroenterology & Motility Disorders. Providers at these centers will be informed of this study and the inclusion and exclusion criteria being used to find eligible participants. These providers will screen their patients for eligibility and inform patients and their parents about our study. Providers will then refer the patient to our research staff, who will reach out to the patient’s parents or guardian and schedule an initial appointment with them. At the initial meeting, participants will be screened for eligibility again, and if still eligible, will be provided with the benefits and risks of the study, and be informed of the possibility of being randomized to the control group. If the participant and guardian agree to enroll in the study, informed consent forms and a baseline characteristics survey will be completed before the end of the first meeting. Study participants will be recruited over a six-month period.

3.4 Subject Protection and Confidentiality

Prior to beginning recruitment, our team will obtain Yale Institutional Review Board (IRB) approval. Our study has been designed per IRB policy 310 concerning the participation of children in research. Children who have agreed to participate in our study will be required to complete the Child’s Assent for Being in a Research Study Form (Appendix A), which explains the study in terms the child can understand and informs them of who they can ask if they have any questions or concerns. Parents or guardians will be required to complete the Parental Permission Form (Appendix B) which includes a more in-depth description of the study, the information they can and cannot share about

the study, and information on how study data is used and kept confidential. All forms will be signed electronically. A research coordinator will be present during the signing of consent forms to explain the purpose of the consent form and to answer any questions the participant or parents/guardian may have. At this time the participants and parent/guardians will also be informed that they are allowed to withdraw from the study at any time.

All research staff will be required to complete Health Insurance Portability and Accountability Act (HIPAA) training and Yale Human Subjects Protection training, protecting the participant's identity and personal health information. The websites containing the yoga instruction and access to surveys will be password protected to ensure only the participant and parent/guardian can access the instruction. All responses to study surveys will be de-identified and encrypted on a computer database only accessible to the research staff responsible for compiling and analyzing data.

3.5 Study Variables and Measures

3.5.1 Treatment Intervention and Control Group

The independent variable is online interactive yoga therapy, as an adjunct therapy to the participant's standard medical care. Yoga sessions will be required three times weekly for 30 minutes. Participants may not go over these requirements within the intervention period. Each session consists of 10 three-minute videos with an instructor demonstrating a single pose and talking through the breathing and imagery portion of the exercise. The videos will also include animations to better help the participants visualize how they should be moving and feeling. Children randomized to the intervention group will perform all 20 possible poses and movements at the first in-person yoga session

under the supervision of a certified child yoga instructor, and then have the option to pick the type and order of the moves they prefer before each at-home session. Parent or guardian supervision will be required when participants perform the poses at home to ensure participant safety. After the 12-week intervention period, participants randomized to the yoga intervention may access the yoga website if they wish, and there is no maximum time or day constraints.

The control group will continue their standard medical care only, which includes current pharmacological treatments and dietary regimens, along with regular appointments with their primary care provider and gastroenterologist.

3.5.2 Primary Outcome Measures

The primary dependent variable will be the Pain Intensity Score, measured using the 6-face Faces Pain Scale-Revised (FPS-R), located in Appendix D. The scale ranges from no pain (0) to very much pain (10). Ratings on the Faces Pain Scale-Revised will be recorded by participants 3 times a day for 1 week at 4 separate times: the week prior to intervention start (week 0), the last week of the intervention period (week 12), and the week of the 6 and 12-month follow-ups. The scores in each week will be averaged to create the Pain Intensity Score. Both the intervention and control groups will record these scores at each time point.

The primary outcome will be the mean difference in Pain Intensity Scores at baseline and 12-month follow-up, compared between the intervention and control groups. The reduction in Pain Intensity Score from baseline to 12-month follow-up will indicate clinical improvement.

3.5.3 Secondary Outcome Measures

A number of secondary dependent variables will be measured in this study. School absenteeism will be recorded at all time points in both groups with the percentage of children that had school absences at least once a month being measured. Quality of life will be measured using the Child (8-12) and Parent Reports of PedsQL GI symptoms module (Appendix E). Quality of life will be measured at baseline, post-intervention and at follow-ups. Pain frequency will be measured using a standardized Pain Frequency Score (PFS): 0 = no daily pain, 1 = 0–20 minutes of daily pain, 2 = 20–40 minutes of daily pain, 3 = 40–90 minutes of daily pain, and 4 = >90 minutes of daily pain. Pain frequency will be measured in both groups at the same time that the primary outcome is recorded, to determine a mean weekly Pain Frequency Score. Finally, the intervention group will record at the 6 and 12-month follow-up whether they have continued to practice yoga after the intervention period or not. Reduced school absenteeism, increased scoring on the PedsQL GI Symptoms module, and reduced pain frequency scores will indicate outcomes with clinical improvement.

3.5.4 Baseline Variables

In order to avoid confounding variables and to determine if randomization was successful, additional participant data will be collected and analyzed. This data includes participant age, gender, race, Rome IV diagnosis (IBS, Functional Dyspepsia, Abdominal Migraine, a combination or Functional Abdominal Pain-Not Otherwise Specified), duration of symptoms (<1 year, 1-2 years, 2-5 year, >5 years), other functional symptoms (headache, back pain, neck pain, tiredness), and household income. See Appendix C for the sample sociodemographic survey form.

3.6 Methodology Considerations

3.6.1 Blinding of Intervention

Study participants cannot be blinded to the group they are randomized to due to the nature of this study. However, primary investigators and other research staff will be blinded to participant group assignment. The yoga instructor will see participants allocated to the yoga intervention group at the initial yoga sessions, and will be instructed not to discuss identifying information about participants with any of the other research staff.

3.6.2 Blinding of Outcome

Outcome surveys via a secure online database prevent the need for research staff to know participant allocation, except for two research assistants one to de-identify participant data and one to complete computerized randomization. This staff member, along with participants will be instructed to not tell other research staff which participants were allocated to which group. Other research staff can analyze the results of this study only after the results have had any identifying information removed.

3.6.3 Assignment of Intervention

Participants who meet all inclusion and exclusion criteria and consent to be a part of the study will then wait to be assigned to a study group. Our study will use block randomization stratified by duration of symptoms in months. We will have a separate research assistant in charge of block assignment and accessing the computer database that will randomly place participants into either an online yoga with SMC group or just SMC group. Once all participants are randomized, they will be sent an email to inform them of group assignment and the next steps of the study process.

3.6.4 Adherence

Tracking of participation in the yoga intervention will be recorded by the yoga website. The website will track the number of moves out of 10 that are completed in each session, along with how many sessions are attended out of the 36 required in the 12-week intervention period. measured as the percentage of participants who complete 100% of the required yoga sessions and the percentage of participants who complete 70% of the required yoga sessions.

The parent permission consent form will suggest their child practice yoga at a similar time and day of the week in order to establish a routine. If a routine is set, it is less likely that participants will forget to partake in the intervention. Participants will also receive an email reminder if the yoga website is not accessed for over 72 hours.

To maintain adherence in the control group, participants will be informed that those who are randomized to the control group will have access to the yoga website once the last follow-up at 12-months is complete.

For the yoga intervention, transportation costs will be reimbursed for the initial in-person yoga session. In addition, all participants will receive a \$50 gift card upon completion of the 12-week intervention period, with an additional \$50 given for completing the 6 and 12-month follow-up surveys.

3.7 Data Collection

During the intervention and follow-up periods, there are numerous surveys to be filled out, with some differences between which surveys the participant receives based on group assignment. See Table 2 for more detail on which surveys are released at certain points in the study timeline. Surveys will be available on a secure database, and

participants will receive an email when surveys are available to be filled out. One research assistant will be in charge of sending out surveys to participants, as well as sending out reminders via email or telephone if the participant does not complete the survey within 48 hours of the survey being sent. The only survey completed in person is the initial sociodemographic survey, completed at the screening meeting with research staff.

Table 2: Timeline of Assessments

	Socio-demographic Survey	Pain Intensity Scale ^A	Peds QL GI Symptoms Score	School Absenteeism	Pain Frequency Score ^A	Continuation of Yoga beyond Intervention Period*	Yoga Adherence*
Screening	█						
Baseline (Week 0)		█	█	█	█		█
End of Intervention (Week 12)		█	█	█	█		█
6 Month Follow-Up		█	█	█	█		
12 Month Follow-Up		█	█	█	█		

* : Collected from Intervention Group participants only

A : Collected three times daily during week of data collection

3.8 Sample Size Collection

The sample size estimation was made with a sample size t-test calculator¹ to compare two independent means for a two-sided alpha of 0.05 and power of 80%. We first calculated the expected decrease in pain intensity score for the intervention group versus the control group using a previous study that also used the Faces Pain Scale-Revised. We found a 52.9% decrease in baseline pain intensity score in the intervention group and an expected 25% decrease in baseline pain intensity score in the control group.²

However, this study used a scale of 0-5, while our study was going to use a scale of 0-10. This meant we needed a study that used Faces Pain Scale-Revised with the same scaling as our proposed study in order to have an expected baseline pain intensity value. We did find a study where researchers were investigating if children with FAPDs had reduced pain with exposure-based cognitive behavioral therapy. The average baseline Faces Pain Scale-Revised score was 5.80.³ This results in an expected mean change in Pain Intensity Score of 3.07 in the intervention group and 1.45 in the control group of our proposed study. The expected effect size for mean change in pain intensity score from baseline to 12-month follow-up between intervention and control groups is therefore 1.62 ± 2.97 . To detect this change in mean pain intensity score, 106 participants would be needed with 53 in each arm. Appendix F provides additional detail on this calculation.

To correct for loss to follow-up, the most conservative attrition rate of the reviewed studies, 32.9%, was assumed.⁴ Therefore, an additional 36 participants were added for a total of 142 participants total with 71 in each arm.

3.9 Analysis

Intention-to-treat analysis will be utilized for all outcome data in order to reduce the effects of dropout and loss to follow-up. For all participants, baseline characteristics will be analyzed between the intervention and control group to control for any confounding variables. For comparison of the means of continuous variables (age, duration of symptoms in years, baseline mean Pain Intensity Score, mean Pain Frequency Score and PedsQL GI symptoms module score), a student t-test will be used. For comparison of categorical variables (gender, race, household income, Rome IV diagnosis, other functional symptoms, baseline school absenteeism), Chi-Square tests will be used,

or Fisher Exact Test if any category contains less than 5 participants. P-values less than or equal to 0.05 will be considered statistically significant.

The primary outcome, mean difference in Pain Intensity Score from baseline to 12-month follow-up for the intervention group will be compared to the control group with a student t-test. To study within-group effects, repeated measures analysis of variance (ANOVA) will be performed to compare participant baseline pain intensity scores with their scores at post-intervention, 6 and 12-month follow-up for both the intervention and control groups. If either group has a statistically significant difference with repeated-measures ANOVA, a paired t-test will be done to determine which time points have the statistically significant mean difference in pain intensity scores. P-values less than or equal to 0.05 will again be considered statistically significant.

The secondary outcomes of school absenteeism (percentage of participants with a school absence at least once a month) and continued yoga practice from baseline to 12-month follow-up will be compared and measured with a Chi-square test. Quality of life scores measured by the Child (8-12) and Parent Reports of PedsQL GI symptoms module will use a student t-test when comparing intervention and control groups at different time points, and repeated-measures ANOVA when comparing within-group changes from baseline to post-intervention or follow-up.

3.10 Timeline and Resources

Once IRB approval is granted, the entire study will be completed within the required two-year limit. One month will be allotted for research staff training and the development of the yoga therapy website. Recruitment will last for six months with the intervention period commencing directly afterward for approximately 3 months. Follow-

up data collection will be performed at 6 and 12-months from the end of the intervention period. Data analysis will be completed in the final two months. See Tables 3 and 4 below for more detail on the study timing.

This study’s research staff will be led by the principal investigator, Ricardo Arbizu MD, MS, and co-principal investigator, Olivia Hollyer, PA-SII. A website creator will be hired to create the website for the yoga. A certified children’s yoga instructor will be hired to teach the initial yoga class for those assigned to the intervention group and to be filmed demonstrating the yoga poses for the website. The yoga instructor may film the yoga poses from any place that is convenient to them, and the initial yoga class will take place at two yoga studios, one in each New Haven and Hartford County on the same day, in order to reduce travel time for participants. Other research staff will include a research coordinator to assist in recruitment, enrollment and consenting of participants, a research analyst to analyze study results, and three research assistants: one to help randomize participants to the study groups, one to send out and monitor completion of surveys, and another to deidentify and compile study data. Research staff and study participants will be compensated for their contributions to the study.

Table 3: Timeline for Study Completion

Month	Website Creation and Training	Recruitment	Data Collection	Data Analysis
1	█			
2		█		
3		█		
4		█		
5		█		
6		█		
7		█		
8			█	
9			█	
10				█



Table 4: Timeline of Intervention Period

Week	Baseline Data Collection	Intervention with No Data Collection	End of Intervention Data Collection
0	█		
1-11		█	
12			█

3.11 References

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3. Lalouni M, Olén O, Bonnert M, Hedman E, Serlachius E, Ljótsson B. Exposure-Based Cognitive Behavior Therapy for Children with Abdominal Pain: A Pilot Trial. *PLOS ONE.* 2016;11(10):e0164647.
4. Evans S, Lung KC, Seidman LC, Sternlieb B, Zeltzer LK, Tsao JC. Iyengar yoga for adolescents and young adults with irritable bowel syndrome. *J Pediatr Gastroenterol Nutr.* 2014;59(2):244-253.

CHAPTER 4: CONCLUSION

4.1 Advantages and Disadvantages

In the past fifteen years, researchers have studied the efficacy of yoga for improving quality of life and abdominal pain in children who suffer from functional abdominal pain disorders. While these studies found clinically significant evidence that yoga therapy can be a helpful adjunct therapy for this population, adherence to yoga therapy was consistently low.^{1,2} Reasons for low adherence included the burden of transportation cost and time on participant families, and yoga programs not designed with children in mind.¹⁻³ There was also a discrepancy in these studies about how long the effects of the yoga therapy lasted after the intervention period ended.

Our study will be the first randomized controlled trial to compare an online yoga therapy as an addition to standard medical care to standard medical treatment only in children ages 8-12 with FAPDs. By better tailoring the yoga therapy for children and allowing participants to adjust the yoga poses they perform in each session, we aim to increase adherence to the intervention. By compensating the control group for their participation and informing them of their ability to access the yoga therapy after the study is complete, we expect to have less control group loss to follow-up compared to previous studies. The improved adherence and loss to follow-up of our study, along with a larger sample size, will increase the generalizability of the results. By controlling for confounding variables and blinding research staff to participant group allocation, our study will also have strong internal validity. We also aim to reduce possible placebo effects in the yoga intervention group by having participants perform yoga poses alone

with parent supervision, eliminating the group support setting that may contribute to falsely improved results in the yoga intervention groups of previous studies.

Several limitations exist in our study. The first is that we cannot blind participants to their group assignment, which increases the possibility of participant expectancy bias. We aim to reduce this bias by blinding participants to certain aspects of the study, including what the study hypothesis is, which will also reduce demand characteristic bias. Another limitation is the self-report nature of many of our primary and secondary dependent variables. Pain and quality of life are experienced by everyone differently, but our study design is focused more on the changes in these outcome measures from baseline to 12-month follow-up. Finally, our study participants will all be from a fairly urban area with access to resources such as a gastroenterologist. The effect of online yoga therapy in children with FAPDs from more rural and lower resource areas should be investigated in future studies to further improve the generalizability of this therapy.

4.2 Clinical and Public Health Significance

Children with FAPDs currently do not have a gold-standard treatment, and current therapies often do not adequately reduce abdominal pain and gastrointestinal symptoms. Uncontrolled episodes of symptoms lead to increased school absence and as a result loss of participation in sports and social groups. Children with FAPDs with poor treatment are at risk of developing chronic pain and/or anxiety and depression in adolescence and adulthood. If the results of this proposed study were to indicate that yoga instruction given online could improve abdominal pain and school participation of children with FAPDs, clinicians could recommend this therapy to children who are struggling to manage their symptoms as a possible adjunct to current treatment.

There is also the opportunity for children with functional pain disorders to receive care from anywhere, even in remote areas where yoga instructors and healthcare facilities are not close by. The use of telemedicine in this way allows for patients to receive care while being in a comfortable environment, and without putting an extra burden on parents. This form of therapy could also be a backup in the case that a child is out-of-town, or if community health conditions prevent in-person contact. ³

4.3 References

1. Evans S, Lung KC, Seidman LC, Sternlieb B, Zeltzer LK, Tsao JC. Iyengar yoga for adolescents and young adults with irritable bowel syndrome. *J Pediatr Gastroenterol Nutr.* 2014;59(2):244-253.
2. Hogstrom S, Philipson A, Ekstav L, et al. Dance and yoga reduced functional abdominal pain in young girls: A randomized controlled trial. *Eur J Pain.* 2022;26(2):336-348.
3. Evans S, Seidman LC, Lung K, Sternlieb B, Zeltzer LK. Yoga for Teens With Irritable Bowel Syndrome: Results From a Mixed-Methods Pilot Study. *Holist Nurs Pract.* 2018;32(5):253-260.

APPENDICES

Appendix A: Child Assent Form

Child's Assent for Being in a Research Study Yale University

Title: Online Yoga for Children with Functional Gastrointestinal Disorders

Why am I here?

We are asking you to take part in a research study because we are trying to learn more about a new online yoga program for kids. We are inviting you to be in the study because we are going to try this program with a specific group of children with gastrointestinal pain, and your doctor thought you could be a good candidate to possibly receive this therapy.

What will happen to me?

If you and your parent or guardian agree, you will be asked to fill out several surveys a week at a time at several different time points in the future, the last being over a year from now. You may be participating in the online yoga program during the survey period, or you may be asked to continue your usual routine, and then receive the online yoga program after the survey period. Either way, if you agree to participate in this study, you will have access to the online yoga program soon or in the future.

If you are asked to participate in the online yoga program during the study period, you will have your first yoga class in-person with an instructor who will teach you all of the poses and will help you perform the poses safely. After this session, all yoga will be practiced at home in a space you are comfortable in, and you will follow along with the same instructor through website videos. You will have the option of choosing which yoga poses you want to do and in which order you wish to do them. You can change the order and type of poses before every yoga session.

Will the study hurt?

This study is not supposed to hurt you. Yoga is a slow and calming therapy that is not meant to be hard or painful. Your parent or guardian will watch you perform the yoga moves to make sure you are safe. This study does not require you to receive any shots or blood tests outside of your usual check-ups from your pediatrician.

Who will know that I am in this study?

Only you, myself, and your parents or guardians will know you specifically will be in the study. If you agree to participate in the study, your name will be replaced with an identification number, so no one else on the research team will know your name or if you are currently in the online yoga program, or will be continuing your usual routine. The online yoga program and the surveys you will fill out are on password-protected websites, so it's important to not share passwords with anyone besides your parents or

guardians. If this study is published, results of the study based on your survey responses would be published, but none of your personal information would be published.

What if I have any questions?

You can ask any questions that you have about the study now. If you have a question later that you didn't think of now, you can call or email a member of the research team.

Do my parents know about this?

This study was explained to your parents and they said that you could be in it. You can talk this over with them before you decide.

Do I have to be in the study?

You do not have to be in the study. No one will be upset if you don't want to do this. If you don't want to be in this study, you just have to tell them. You can say yes now and change your mind later. It's up to you.

Writing your name on this page means that you agree to be in the study, and know what will happen to you. If you decide to quit the study all you have to do is tell the person in charge.

Signature of Child

Date

Signature of Researcher

Date

Appendix B: Sample Parental Consent Form

PARENTAL CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL

Study Title: Online Yoga for Children with Functional Gastrointestinal Disorders: A Randomized Control Trial

Principal Investigator: Ricardo Arbizu, MD, MS

Funding Source: Pending

Invitation to Participate and Description of Project

You and your child are invited to participate in a research study designed to investigate a new online therapy, yoga, in the treatment of pediatric functional abdominal pain disorders. You have been asked to participate because your child meets the Rome IV criteria for a functional abdominal pain disorder, is between the ages of 8-12, and has not been ruled ineligible based on our study's exclusion criteria. Your child's clinician has identified you and your child as possible participants for this study from either the Yale Pediatric Gastroenterology Outpatient Center or the Connecticut Children's Center for Neurogastroenterology & Motility Disorders. Approximately 140 participants will be recruited for this study.

To decide whether or not you wish to be a part of this research study, you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the research study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Description of Procedures

If you and your child agree to participate in this study, you will be requested to fill out a sociodemographic survey today that asks for more information about your child's health and background. After you and your child are officially recruited into the study, your child will be randomly assigned via a computer program to either the intervention or control group. The intervention group will receive the online yoga intervention alongside standard medical care for 12 weeks followed by optional use for 12-months, while the control group will continue their standard medical care for the 12-week intervention period and following 12-months. Standard medical care is the child's usual regimen of pharmacotherapy, diet and clinician support that they were already utilizing before being recruited for our study. Those assigned to the control group will have full access to the online yoga program following the conclusion of the study.

Those assigned to the online yoga intervention will be required to practice yoga three times a week for 30 minutes during the 12-week intervention period. When during the week this intervention is performed is based on participant and parent preference, but a similar time and day of the week should be maintained throughout the intervention period if possible. The first yoga session will be in-person so that participants can learn the 20 yoga poses safely and accurately from a certified child yoga instructor. The online yoga therapy will be accessible via a password-protected website. Upon the first login to the website, a tutorial will guide you and your child through how to access the program and change the program to the child's preferences. The website will record how many sessions your child completes. Online yoga practice will be optional beyond the 12-week intervention period.

Surveys measuring participant abdominal pain intensity and frequency, quality of life, school absence, and continued yoga practice (intervention group only) will be accessed via a secure survey database and you will be informed via email when these surveys are available to be filled out. Surveys are required to be filled out within 48 hours of them being released. Surveys will be sent out during the week before the intervention period, the last week of the intervention period, and at 6 and 12-months post-intervention end.

You will be told of any significant new findings that are developed during the course of your participation in this study that may affect your willingness to continue to participate. If this study is published, you will be notified and any personal information you provided during this study will not be included.

Risks and Inconveniences

The risks associated with this study are very minimal. Physical injury during yoga practice is possible if a participant overstretches or falls during a pose. To prevent this, the yoga instructor will observe your child at the first in-person session to ensure the child is performing the poses safely. A parent or guardian will be required to supervise all at-home yoga sessions to monitor participants for risk of falls. The yoga poses selected for this study are intended for children, and so are lower-risk moves compared to those intended for adults.

Since personal information will be collected for recruitment into this study and a sociodemographic survey will be collected today, there is a risk of a breach of confidential information about your child's health and background. However, this risk is low due to the deidentification of participant data and group assignment. Research staff have also all received participant and study confidentiality training.

Benefits

Benefits from this study may include improvements in symptoms related to FAPDs, reduced school absence, improved quality of life, and a new alternative treatment to add to a child with FAPD's regimen if the standard regimen is not working well.

Economic Considerations

Participants will be compensated for their completion of the study, in the form of a \$100 gift card. Participants assigned to the online yoga intervention will be reimbursed for transportation, parking and other costs associated with travel to the first in-person session. According to the rules of the Internal Revenue Service (IRS), payments that are made to you as a result of your participation in a study may be considered taxable income. You will still be responsible for any co-pays required by your insurance company for standard treatment.

Treatment Alternatives/Alternatives

The alternative treatment to being in this study is to decline participation. If you decline to participate in this study, your child's healthcare providers will continue standard treatments and investigate other possible alternatives.

Confidentiality

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as required by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. Participants will be assigned a random identification number, which will be used for the entire study. Once physical personal data has been collected and placed into a secure computer database, it will be destroyed. All intervention materials and surveys are on password-protected websites. When the results of the research are published or discussed at conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained.

All personnel involved in this study are required to abide by the Health Insurance Portability and Accountability Act (HIPAA). Only designated members of the research team are allowed to access identifying personal information. Staff involved in collecting and analyzing results will only know participants by their identification numbers.

The use of video or audio recordings of participants will not be used in this study.

Representatives from the Yale Human Research Protection Program, and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects) may inspect study records during internal auditing procedures. However, these individuals are required to keep all information confidential.

In Case of Injury

If you are injured while in the study, seek treatment and contact the study doctor as soon as you are able.

If you become ill or are physically injured due to the study intervention you will not be responsible for the costs required to diagnose or treat such injury. The costs of diagnosis and medical care for any complication, injury, or illness caused by the study intervention will be covered by the Sponsor as long as you have followed the directions of the study doctor.

If you receive a bill for any costs related to the diagnosis or treatment of your injury, please contact the study doctor.

You will not receive any other kind of payment. There are no plans to pay you for such things as lost wages, disability, or discomfort as part of this study. ***You do not give up any of your legal rights by signing this consent form.***

Voluntary Participation and Withdrawal

Participating in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow the use of your information as part of this study.

If you do become a subject, you are free to stop and withdraw from this study at any time during its course. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. If in the intervention group, you will lose access to the online yoga intervention. If in the control group, you will lose future access to the online yoga program.

The researchers may also withdraw you from participating in the research if necessary. This may be due to a new diagnosis of a more serious disease that needs immediate treatment, diagnosis of an organic functional disorder such as inflammatory bowel disease or celiac disease, hospitalization, or participant non-compliance. Starting any alternative therapy such as cognitive behavioral therapy, hypnotherapy, or other

psychotherapies while participating in either the intervention or control group will also result in removal from the study.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your providers or with Yale School of Medicine.

When you withdraw from the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to ensure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

Name of Parent: _____

Signature: _____

Relationship to Participant: _____

Date: _____

Signature of Principal Investigator

Date

or

Signature of Person Obtaining Consent

Date

If, after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203-432-5919.

If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.

Appendix C: Sociodemographic Survey

Date: __/__/_____

Participant Name: _____

Participant DOB: __/__/__

Parent / Guardian Name: _____

Relation to Participant: _____

Participant Gender (circle one): Female Male Other: _____

Participant Ethnicity (circle one): Hispanic Non-Hispanic

Participant Race (circle one): White / Caucasian Black / African
American Indian Asian / Pacific Islander
Other / Multiracial

Rome IV Functional Abdominal Pain Disorder Diagnosis:

- Irritable Bowel Syndrome
- Functional Dyspepsia
- Abdominal Migraine
- Functional Abdominal Pain – Not Otherwise Specified
- More than one (please list): _____

Duration of Symptoms: ____ years ____ months

Other Chronic Functional Symptoms:

- Headache
- Back Pain
- Neck Pain
- Tiredness / Fatigue

Annual Household Income:

- < \$25,000
- \$25,000 - \$49,999
- \$50,000 - \$74,999
- \$75,000 - \$99,999
- > \$100,000

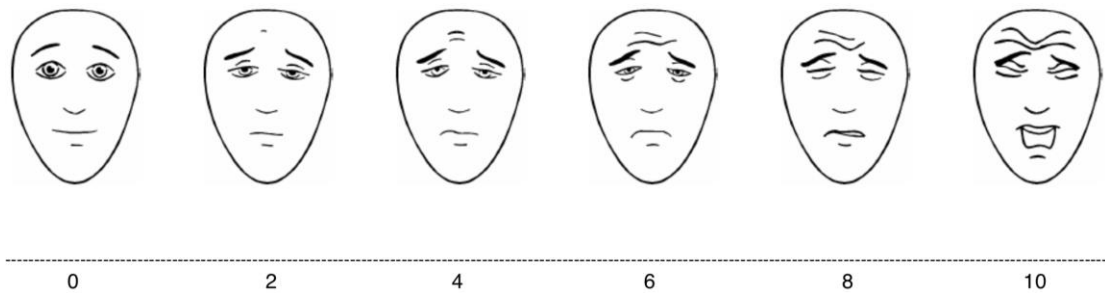
Appendix D: Faces Pain Scale-Revised Form

Faces Pain Scale – Revised (FPS-R)

In the following instructions, say "hurt" or "pain", whichever seems right for a particular child.

"These faces show how much something can hurt. This face [point to face on far left] shows no pain. The faces show more and more pain [point to each from left to right] up to this one [point to face on far right] - it shows very much pain. Point to the face that shows how much you hurt [right now]."

Score the chosen face 0, 2, 4, 6, 8, or 10, counting left to right, so "0" = "no pain" and "10" = "very much pain". Do not use words like "happy" or "sad". This scale is intended to measure how children feel inside, not how their face looks.



Permission for Use. Copyright of the FPS-R is held by the International Association for the Study of Pain (IASP) ©2001. This material may be photocopied for **non-commercial clinical, educational and research** use. For reproduction of the FPS-R in a journal, book or web page, or for any commercial use of the scale, request permission from IASP online at www.iasp-pain.org/FPS-R.

Sources. Hicks CL, von Baeyer CL, Spafford P, van Korlaar I, Goodenough B. The Faces Pain Scale – Revised: Toward a common metric in pediatric pain measurement. *Pain* 2001;93:173-183. Bieri D, Reeve R, Champion GD, Addicoat L, Ziegler J. The Faces Pain Scale for the self-assessment of the severity of pain experienced by children: Development, initial validation and preliminary investigation for ratio scale properties. *Pain* 1990;41:139-150.

Appendix E: Child (8-12) and Parent Reports of PedsQL GI Symptoms Module

PedsQL™ 3.0 Gastrointestinal Symptoms Module



The **Child and Parent Reports** of the **PedsQL™ 3.0 Gastrointestinal Symptoms Module** for:

- Children (ages 8-12),
- Teens (ages 13-18),
- Young Adults (ages 18-25)

are composed of 74 items comprising 14 dimensions.

DESCRIPTION OF THE GASTROINTESTINAL SYMPTOMS MODULE:

Dimensions	Number of Items	Cluster of Items	Reversed Scoring	Direction of Dimensions
Stomach Pain and Hurt	6	1-6	1-6	
Stomach Discomfort When Eating	5	1-5	1-5	
Food and Drink Limits	6	1-6	1-6	
Trouble Swallowing	3	1-3	1-3	
Heart Burn and Reflux	4	1-4	1-4	
Nausea and Vomiting	4	1-4	1-4	
Gas and Bloating	7	1-7	1-7	
Constipation	14	1-14	1-14	Higher scores indicate lower problems.
Blood in Poop (Bowel Movement)	2	1-2	1-2	
Diarrhea	7	1-7	1-7	
Worry About Going Poop (Bowel Movements)	5	1-5	1-5	
Worry About Stomach Aches	2	1-2	1-2	
Medicines	4	1-4	1-4	
Communication	5	1-5	1-5	

SCORING OF DIMENSIONS:

Item Scaling	5-point Likert scale from 0 (Never) to 4 (Almost always)
Weighting of Items	No
Extension of the Scoring Scale	Scores are transformed to a 0 to 100 scale.
Scoring Procedure	<u>Step 1: Transform Score</u> Items are reversed scored and linearly transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0.

	<p>Step 2: Calculate scores by Dimensions</p> <ul style="list-style-type: none"> • If more than 50% of the items in the scale are missing, the scale scores should not be computed, • Mean score = Sum of the items over the number of items answered. <p><u>Symptoms Total Scales Score</u> = Sum of the items over the number of items answered in the 10 Symptoms Scales.</p> <p>Total Score: Sum of all the items over the number of items answered on all the Scales.</p>
<p>Interpretation and Analysis of Missing Data</p>	<p>If more than 50% of the items in the scale are missing, the Scale Scores should not be computed.</p> <p>If 50% or more items are completed: Impute the mean of the completed items in a scale.</p>

Appendix F: Sample Size and Power Calculation

Sample size calculation was conducted using Statulator Sample Size Calculator for Comparing Two Independent Means.

Calculate Visualise Tabulate

Input Values

Select one of the two options to specify input values. Hover over the ? sign to obtain help.

Expected Means ?

Mean of the Reference Group: ?	3.07
Mean of the Test Group: ?	1.45
Standard Deviation: ?	2.97

Expected Difference between Means ?

Click the Options button to change the default options for Power, Significance, Alternate Hypothesis and Group Sizes. Use the Adjust button to adjust sample sizes for t-distribution (option applied by default), and clustering.

▶ Calculate Options Adjust ↻ Reset

Assuming a pooled standard deviation of 2.97 units, the study would require a sample size of:

53

for each group (i.e. a total sample size of 106, assuming equal group sizes), to achieve a power of 80% and a level of significance of 5% (two sided), for detecting a true difference in means between the test and the reference group of -1.6199999999999999 (i.e. 1.45 - 3.07) units.

In other words, if you select a random sample of 53 from each population, and determine that the means of the test and the reference groups are 1.45 and 3.07 units, respectively, and the standard deviation is 2.97 units, you would have 80% power to declare that the two groups have significantly different means, i.e. a two sided p-value of less than 0.05.

Reference: Dhand, N. K., & Khatkar, M. S. (2014). Statulator: An online statistical calculator. Sample Size Calculator for Comparing Two Independent Means. Accessed 13 May 2022 at <http://statulator.com/SampleSize/ss2M.html>

Note: Statulator used the input values of a power of 80%, a two sided level of significance of 5% and equal group sizes for sample size calculation and adjusted the sample size for t-distribution. You may change the options by clicking [here](#) or the 'Options' button and the adjustments by clicking [here](#) or the 'Adjust' button.

To correct for loss to follow-up, the most conservative attrition rate of the reviewed studies, 32.9%, was assumed. Therefore, an additional 36 participants were added for a total of 142 participants total with 71 in each arm.

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